The Office Action

Claims 1-8, 10-13, 15-19, and 58 are pending. Claims 1-8, 10-13, 15-19 stand rejected for anticipation by Hess (U.S. Patent No. 6,326,465; hereafter "Hess") as evidenced by URLs http://us.expasy.org/cgi-bin/protp and http://us.expasy.org/cgi-bin/peptidecutter/peptidecutt. Claim 58 would be allowable if rewritten in independent form.

Rejections under 35 U.S.C. § 102(e)

Claims 1-8, 10-13, 15-19 stand rejected for anticipation by Hess. Applicant respectfully disagrees. M.P.E.P. § 2131 states that "[a] claim is anticipated only if each and every element as set forth in the claims is found ... in a single prior art reference." This standard has not been met in the present case.

Claim 1 (from which all other claims depend) recites:

> 1. A method for stimulating an immune response specific toward a naturally-occurring protein in an animal having an immune system including T cells, said method comprising administering to said animal an altered protein or polypeptide fragment thereof derived from said naturally-occurring protein, wherein an unstable polypeptide segment has been inserted by artifice into said altered protein, wherein said unstable polypeptide segment has an average hydrophobicity value that is lower than the average hydrophobicity value of said altered protein; has a sequence conservation that is lower than a sequence conservation of said altered protein; has an amide protection factor that is lower than 10^4 wherein said altered protein is in a native conformational state; has an average amide protection factor that is lower than the average amide protection factor for said altered protein in a denatured conformational state; has an NMR order parameter (S^2) of less than 0.8; or has an average B-factor value that is higher than the average B-factor value of said altered protein, and wherein

immunogenicity of said naturally-occurring protein is increased. (emphasis added)

Thus, claim 1 requires an altered protein including (1) a naturally occurring protein, or fragment thereof, and (2) an unstable polypeptide sequence inserted by artifice into the naturally occurring protein or fragment.

Hess teaches a method of modulating an immune response by administering a polypeptide including two segments, a portion of the invariant chain of MHC class II and an antigen. Hess states that "chimeric fusion polypeptides can be made using CLIP, or truncated variants thereof, to modulate the immune response to the non-CLIP fusion partner" (col. 3, l. 66 – col. 4, l. 1). Based on this teaching, the Office selected one disclosed CLIP sequence (SEQ ID NO: 5) from Hess and determined that it is unstable and cleaved by a protease according to the ProtParam and Peptide Cutter programs. The Office thus asserts that the CLIP sequence of Hess is equivalent to the unstable sequence required in the instant claims, and that Hess' method of administering a peptide containing a CLIP sequence to modulate an immune response is equivalent to the instantly claimed method.

Although Hess teaches a peptide containing an unstable segment (as measured by ProtParam), Hess does not ever teach modulating an immune system by employing an altered protein or protein fragment containing an unstable sequence inserted into a protein or fragment by artifice, as required in claim 1. The peptides containing a CLIP segment disclosed by Hess are fusion products (see, for example, Example 14; SEQ ID NO: 14), unlike the altered proteins or fragments employed in the instant claims. In general, a

fusion product contains two distinct regions that are joined together end to end. Thus, the peptides employed in the methods of Hess contain a CLIP segment at a terminus of the peptide. In contrast, the altered proteins of the instant claims contain an unstable segment inserted into a naturally occurring protein or fragment thereof. The unstable segment is therefore not located at a terminus of an altered protein or fragment in the instant claims since the segment is located in the interior of the protein or fragment. Since the altered protein or fragment employed in the instant method differs from the fusion peptides of the method of Hess, Hess does not disclose each and every element of claim 1, as required for anticipation, and the rejection of claims 1-11 should be withdrawn.

CONCLUSIONS

Applicant submits that the claims are now in condition for allowance, and such action is respectfully requested. If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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